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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/763,377
Filing Date: January 23, 2004
Appellant(s): OR, YAT SUN

Suanne Nakajima
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 26, 2007 appealing from the Office action mailed December 15, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

(9) Grounds of Rejection

The following ground(s) of rejection as advanced in office actions of record are applicable to appealed claim 1:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the process as instantly claimed using macrolide antibiotic, does not reasonably provide enablement for a process using any macrocyclic compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) The breadth of the claims
(B) The state of the prior art
(C) The level of one of ordinary skill
(D) The level of predictability in the art
(E) The amount of direction provided by the inventor
(F) The existence of working examples
(G) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

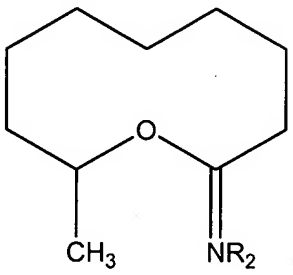
The breadth of the claims

Claim 1 is drawn to a process for making a bridged macrocyclic product comprising reacting a macrocyclic compound having at least two nucleophilic moieties

with a bifunctional bridging component characterized by its ability to form a π-allyl metal complex. The term macrocyclic compound and catalyst are broad and are seen to encompass several macrocyclic compounds other than macrolides recited in instant claim 5 and any other catalyst.

The state of the prior art

The examiner notes that the art cited by the applicants and the prior art of record, teach macrocyclic compounds mainly from the erythromycin class of macrocyclics that have several nucleophilic groups like hydroxyl, epoxy amino, etc., that can form a bridge with a bridging component. There are no examples of bridging being performed with compounds like



Both the oxygen and the nitrogen in the above structure with their electron pairs are seen as nucleophilic moieties (according to the definition of a nucleophile in organic chemistry). With no other leaving groups this macrocyclic compound that has at least two nucleophilic moieties this macrocycle cannot form a bridge with a bridging component as instantly claimed.

The level of predictability in the art

There is not seen sufficient data to substantiate that a bridged product as instantly claimed can be made with any macrocyclic compound comprising any two nucleophilic moieties.

The amount of direction provided by the inventor

The instant specification is not seen to provide enough guidance that would allow a skilled artisan to extrapolate from the disclosure and the examples provided to enable the formation of a bridged product as instantly claimed using any macrocyclic compound comprising any two nucleophilic moieties.

The existence of working examples

The working examples set forth in the instant specification are drawn to formation of a bridged product using erythromycin as the macrocyclic compound, which has nucleophilic groups like hydroxyl, which can form a bridge. Despite these examples there is little enabling disclosure for the same process to be extended to any macrocyclic compound.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure

Indeed, in view of the information set forth, the instant disclosure is not seen to be sufficient to enable the use of any macrocyclic compound in the process as instantly claimed. One of ordinary skill in the art would have to carry out the process in order to determine the type of macrocyclic compound and the type of nucleophilic moiety and the type of catalyst needed to carry out the said process.

(10) Response to Argument

Regarding the rejection of Claim 1 under 35 U.S.C. 112, first paragraph, Applicants' argue that:

1. The Examiner has presented the structure above and states that the oxygen and NR_2 groups that bear an electron pair are nucleophiles and has not provided evidence to support this allegation.

2. One of skill would recognize that the oxygen atom in this structure is not nucleophilic. A nucleophile requires more than the presence of an oxygen. Even if the oxygen were considered a nucleophile the ring oxygen in the structure presented by the Examiner would be positive if a bridge were to form. Such trivalent oxygen is positive and is unstable. The selection of a compound that will fail to form a bridge does not prove that the rejection is proper. Even in cases where it is hard to predict the bridge formation, it would only be a routine experimentation for one of ordinary skill in the art to carry out the process as instantly claimed and determine which macrocycle would be inoperative or operative.

Examiner's Response regarding the 35 U.S.C. 112, first paragraph rejection:

The instant process is drawn to reaction of a macrocyclic compound characterized by the presence of at least two nucleophilic moieties. Atoms or groups that bear an electron pair are also nucleophiles, according to the definition of the term nucleophile, in organic chemistry. One of skill in the art knows this and evidence or support for the same is not seen as necessary. The structure of a macrocyclic compound that has two moieties, oxygen and NR_2, in which the oxygen and the nitrogen atoms both have lone pair of electrons, as shown by the Examiner, falls under the category of a macrocyclic compound having at least two nucleophilic moieties. Even

in structures with a hydroxyl group, wherein the hydroxyl functions as a nucleophile, it is the oxygen of the hydroxy with its lone pair of electrons that acts as a nucleophile. This is also known to one of skill in the art. A macrocycle as shown above cannot form a bridge as instantly claimed. Hence any macrocycle with a nucleophilic moiety as broadly encompassed, will not form a bridge via the reaction as instantly claimed. The instant specification is enabling only for macrolides like erythromycin having functional groups, for example, hydroxyl (with a lone pair of electrons on oxygen), which will form the said bridge. In cases where the formation of such a bridge is hard to predict is when one of skill in the art will have to perform undue experimentation to see if the bridge formation is possible.

The following ground(s) of rejection as advanced in office actions of record are applicable to appealed claims 1-12:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Or et al (WO 99/21864)

Or et al teaches a process for making a bridged macrocyclic compound (formula 14, page 36) comprising the reaction of the macrocyclic compound of formula 1 (page 34, has at least two nucleophilic groups) with the bridging components H_2N-$(CH_2)_m$-A-B-D-X and $(CH_2)_2$-C=CH_2 (the second bridging component with the double bond forms a pi-allyl complex with a metal; page 36, scheme 3) to yield the bridged product. Both these bridging components have the

nucleophilic moieties and the double bond capable of forming a pi-allyl complex as instantly claimed. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or (formula 1, page 34) has two sugar units attached to it. The macrocyclic compound of Or has an ethyl group attached to the carbon adjacent to the ring oxygen. This is the group L in structure I in instant claim 6. It also has a second carbonyl group (at the top left of formula 1, page 34), which corresponds to X and Y in instant claim 5 taken together to form a carbonyl group.

However, Or et al teach the use of two separate bridging components to form the bridged product instead of a single bifunctional bridging component as instantly claimed. But the two individual bridging components have a functional group on one end through which the attachment to the macrocyclic compound is achieved. One of them also has a double bond, which has the ability to form a pi-allyl metal complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process of Or to make a bridged macrocyclic product as instantly claimed using a single bifunctional bridging component as instantly claimed since the starting material, the bridging components having the structural limitations similar to one instantly claimed and the process steps as instantly claimed is seen to be taught in the prior art.

Regarding the rejection of Claims 1-12 under 35 U.S.C. 103(a), Applicants' argue that:

1. The overall process disclosed in the WO '864 document provides different bridged compounds than presently claimed.

2. The prior art process involves attaching two individual components to the macrocycle and then coupling the two together to form the bridge. The assertion by the Examiner that the two individual components can be coupled before attaching it to the macrocyclic compound is obvious is erroneous.

3. The process suggested by the Examiner would be expected to reduce efficiency based on possible side reactions. It is not clear how a process, which is expected to lower the yield resulting from complex mixtures, can make obvious a process, which resulted in a high yield.

Examiner's Response regarding the 103(a) rejection:

1. The process disclosed in WO '864 is one for making a bridged macrocyclic compound as instantly claimed. The macrocyclic compound and the bridging components, which have nucleophilic moieties and a double bond capable of forming a pi-allyl metal complex, disclosed by WO '864 also meet the limitations of the instant claims. The instant claims are not drawn to a specific type of bridged compound that is distinct from that disclosed in the prior art.

2. The prior art process involves attaching two individual components, both of which meet the limitations of the instant claims, to the macrocycle and then coupling the two together to form the bridge. One of skill in the art will recognize that the same type of bridging can be achieved by having all the structural limitations of the bridging group in a single component, i.e. having the bridging group bifunctional and also having a double bond that can form a complex with a metal. It is well within the purview of one of skill in the art to recognize this from the teachings of the prior art. The prior art need not explicitly teach this. So, making the compound as instantly claimed is an obvious variant and can be recognized and performed based on the choice of experimental design. Hence, to choose a method of achieving the bridging step similar

to the one disclosed in the prior art (the end result being the same-bridging) by recognizing the alternative method that is within the skill level of the artisan is not seen as erroneous.

3. Side reactions are possible in many organic reactions, including the method as instantly claimed by the applicants and is not unique to the one suggested by the Examiner. This fact is also known to one of skill in the art. Moreover side reactions in general need not necessarily reduce the yield to such an extent that the process step is not worth doing. The formation of a bridge using a bridging component that has the structural limitations in a single component would be expected by the skilled artisan to give the same good yield as reported in the prior art using two individual components, if not higher. There is a reasonable expectation of success. So, the assertion by the applicants that the process suggested by the Examiner, which is forming a bridge as instantly claimed, would be expected to reduce efficiency based on possible side reactions is not justified and is not supported by evidence either.

Hence, the process of Or as disclosed in WO '084 is similar to the one instantly claimed and achieves the same result as instantly claimed and does render the instant claims obvious.

The Examiner has presented arguments above addressing the argument of the applicants.

For the reasons discussed above, it is believed that the rejections should be sustained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

Ganapathy Krishnan
Patent Examiner, AU 1623
July 05, 2007
Conferees:

10/1/07

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